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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/215,163	12/18/1998	JEFFREY R. STINSON	04995.0032-0	7721

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/215,163	STINSON ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,14,17-20,23,29 and 32-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,14,17-20,23,29 and 32-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-25-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10-25-2004 has been entered.

The amendment and response filed on 10-25-2004 are acknowledged. Claims 1, 2, 14, 17-18, 20, 29 and 38 have been amended. Claims 44-55 have been added. Claims 1, 2, 14, 17-20, 23, 29 and 32-55 are pending and currently under examination.

Claim Rejections Withdrawn

The rejection of claim 20 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of term "variable region contains at least part of the CDR sequences located as follows..." is withdrawn in light of the amendment thereto.

The rejection of claims 1, 2, 14, 17-20, 23, 29 and 32-43 under 35 U.S.C. 103(a) as being unpatentable over Spiers et al. (Canadian Journal of Microbiology, 1991, Vol. 37, pages 650-653) or O'Brien et al. (U.S. Patent 5,747,272) in view of Carter et al. (WO 94/04679) is withdrawn in lieu of the rejection set forth below.

The rejection of claims 1, 2, 14, 17-20, 23, 29 and 32-43 under 35 U.S.C. 103(a) as being unpatentable over Spiers et al. (Canadian Journal of Microbiology, 1991, Vol. 37, pages 650-

653) or O'Brien et al. (U.S. Patent 5,747,272) in view of Shitara et al. (U.S. Patent 5,866,962) is withdrawn in lieu of the rejection set forth below.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claim 41 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 5,747,272 is maintained for reasons of record. Applicant has indicated that they address said rejection once there is indication of allowable subject matter.

Claims 1-2, 14, 17-20, 23, 29 and 32-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 5,747,272 in view of Carter et al. (WO 94/04679) is maintained for reasons set forth in the

rejection of claims 1-2, 14, 17-20, 23, 29 and 32-43 in the previous Office action. Applicant has indicated that they address said rejection once there is indication of allowable subject matter.

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 2, 14, 17-20, 23, 29, 32-40 and 42-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for humanized monoclonal antibodies based on monoclonal antibodies 13C4 or 11E10 (**defined regions**), does not reasonably provide enablement for humanized antibodies "containing at least part of a murine immunoglobulin variable region as shown in Figure 3 (SEQ ID NO:21 or Figure 6 (SEQ ID NO:42), wherein the antibody specifically reacts with Stx1 or Stx2 antigen or portions of SEQ ID NO:42 or SEQ ID NO:44 for the reasons set forth in the previous Office action in the rejection of claims 1, 2, 14, 17-20, 29, 32-40 and 42-43. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

Applicant argues:

1. The specification clearly sets forth the sequences of the variable regions as well as specific complementary determining region (CDR) sequences required to confer binding to Shiga toxin protein.

2. All the claimed humanized antibodies recite sequences based on the defined regions of monoclonal antibodies 13C4 and 11E10 which are acknowledged to be enabled by the instant specification.

3. Any "experimentation" involved in isolating and characterizing variable regions is straightforward.

4. The Examiner's requirement for Applicant to include specific epitope sequences has no basis in law.

5. No scientific evidence has been provided that establishes a basis for doubting the enablement of the instant invention.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1-5, undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

Breadth of the claims

The rejected claims are drawn to a genus of humanized antibodies, the members of which specifically reacts with the Stx1 or Stx2 antigen wherein said antibodies contain "at least part of " a given immunoglobulin variable region. Consequently, said antibodies must share only a single amino acid with said variable region.

Working Examples/Guidance of Specification

The specification fails to describe immunoepitopes against which the claimed antibodies are raised and must subsequently bind. The working examples disclose specific antibodies that meet the limitations of the instant claims. However, these "examples" are not sufficient to provide enablement for the full scope of the rejected claims.. The specification is silent as to what specific "immunoepitope" confers said a given immune response.

State of the prior art and Unpredictability of the art

The specification outlines the materials and methods needed to make humanized antibodies utilizing the 13C4 or 11E10 monoclonal antibodies. However, the specification is silent on the sequences of the murine variable region required to confer function on the chimeric antibody the location (or sequence) of the immunogenic epitopes. Given the lack of guidance contained in the specification and the unpredictability in determining acceptable sequence variations, one of skill in the art could not make the broadly claimed invention without undue experimentation. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome **and form immunoepitopes**. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein,

the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally, Greenspan et al. (*Nature Biotechnology* **17**: 936-937, 1999), disclose defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. This constitutes undue experimentation. Therefore, given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of a directed immune response, the specification, as filed, is only enabling for only the specific antibodies disclosed in the specification that are produced from monoclonal antibodies13C4 or 11E10. Finally it should be noted that while Applicant asserts that the claimed antibody must bind antigen, claims 1 and 44-45 merely require that the claimed antibody "specifically reacts" with Stx1 or Stx2 antigen.

Claims 23, 29, 39-40 and 44-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions comprising

humanized monoclonal antibodies based on monoclonal antibodies 13C4 or 11E10 (**defined sequences**), does not reasonably provide enablement for pharmaceutical compositions comprising humanized antibodies "containing at least part of a murine immunoglobulin variable region as shown in Figure 3 (SEQ ID NO:21 or Figure 6 (SEQ ID NO:42), wherein the antibody specifically reacts with Stx1 or Stx2 antigen or portions of SEQ ID NO:42 or SEQ ID NO:44 for the reasons set forth in the previous Office action in the rejection of claims 23, 29 and 39-40. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

Applicant argues:

1. The enablement rejection as it pertains to "pharmaceutical compositions" is in reality a utility rejection and should be addressed under the Utility Examination Guidelines.

2. The specification (Example 8) demonstrates the efficacy of the humanized 13C4 and 11E10 antibodies.

With regard to Point 1, enablement not utility is the correct basis of the rejection.

With regard to Point 2, the specification only provides examples of humanized 13C4 and 11E10 antibodies, which are set forth in the rejection as being enabled. However, the specification is silent on how any other of the claimed antibodies would be used and equally silent on the efficacy of a given composition. Hence, since no evidence has been provided that illustrates or even suggests that the full breadth of the claimed pharmaceutical compositions are capable of eliciting a beneficial therapeutic response, one of skill in the art would not be able to make and use the claimed invention.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 14, 17-20, 23, 29, 32-40 and 42-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to a genus of humanized antibodies, the members of which specifically reacts with the Stx1 or Stx2 antigen wherein said antibodies contain "at least part of" a given immunoglobulin variable region. Consequently, said antibodies must share only a single amino acid with said variable region.

The courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims

to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

In the instant application, Applicant has failed to "fully characterize" the antigen (Stx1 and Stx2) to which the claimed antibody binds. The instant claims are drawn to all antibodies or fragments thereof with specificity to any Shiga toxin proteins generally, or Stx1 and Stx1 specifically, as long as said antibody comprises "at least a part of" a given immunoglobulin variable region. This includes Fab fragments that have limited immunological properties as compared to intact monoclonal antibodies. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met.

The specification does not describe with any degree of specificity the Shiga toxin proteins to which the members of the claimed genus of antibodies must bind in order to achieve the desired immunological response, such that the specification might reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings

or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

As evidenced by Greenspan et al. (*Nature Biotechnology* **17**: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an

antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed.

In conclusion, only the specific antibodies disclosed in the specification that are produced from murine antibodies 13C4 and 11E10 meet the Written description requirement.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 14, 17-20, 23, 29 and 32-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Edwards et al. (V110/11:113 page 113, 1997 – IDS).

Edwards et al. disclose humanized forms of the 13C4 and 11E10. It is deemed, in absence of evidence to the contrary, to have all the structural and immunological properties recited in the instant claims.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 14, 17-20, 23, 29 and 32-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiers et al. (Canadian Journal of Microbiology, 1991, Vol. 37, pages 650-653) or O'Brien et al. (U.S. Patent 5,747,272) in view of Carter et al. (WO 94/04679) and Tzipori et al. (U.S.2003/0082189 A1 – IDS).

Spiers et al. and O'Brien disclose the 11E10 and 13C4 antibodies.

They differ from the instant invention in that they don't disclose humanized forms of said antibodies.

Carter et al. disclose the methods of producing humanized antibodies.

Tzipori et al. disclose that monoclonal antibodies specific for Shiga toxins (i.e. like 13C4 and 11E10) can be used to treat hemolytic uremic syndrome (see abstract).

Consequently, it would have been equally obvious for one of skill in the art to employ the methodologies disclosed by Carter et al. to humanize the 13C4 and 11E110 antibodies in order to reduce the side effects associated with anti-mouse immunoglobulins since the process of humanizing a known antibody is well known in the art. One would have been motivated to humanize said antibodies in order to use them in the treatment methodologies disclosed by Tzipori et al.

One would have had a reasonable expectation of success as humanizing antibodies is a well-established method within the art. Furthermore, though the sequences of said antibodies where not explicitly disclosed it would have been standard practice for one of skill in the art to obtain said sequences utilizing standard sequencing methods.

Claims 1, 2, 14, 17-20, 23, 29 and 32-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiers et al. (Canadian Journal of Microbiology, 1991, Vol. 37, pages 650-653) or O'Brien et al. (U.S. Patent 5,747,272) in view of Shitara et al. (U.S. Patent 5,866,692) and Tzipori et al. (U.S.2003/0082189 A1 – IDS).

Spiers et al. and O'Brien disclose the 11E10 and 13C4 antibodies.

They differ from the instant invention in that they don't disclose humanized forms of said antibodies.

Shitara et al. disclose the methods of producing humanized antibodies.

Tzipori et al. disclose that monoclonal antibodies specific for Shiga toxins (i.e. like 13C4 and 11E10) can be used to treat hemolytic uremic syndrome (see abstract).

Consequently, it would have been equally obvious for one of skill in the art to employ the methodologies disclosed by Shitara et al. to humanize the 13C4 and 11E110 antibodies in order to reduce the side effects associated with anti-mouse immunoglobulins since the process of humanizing a known antibody is well known in the art. One would have been motivated to humanize said antibodies in order to use them in the treatment methodologies disclosed by Tzipori et al.

One would have had a reasonable expectation of success as humanizing antibodies is a well-established method within the art. Furthermore, though the sequences of said antibodies where not explicitly disclosed it would have been standard practice for one of skill in the art to obtain said sequences utilizing standard sequencing methods.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ROBERT A. ZEMAN
PRIMARY EXAMINER

November 27, 2006